

***I. Elections/Restrictions***

On page 2 of the Office Action, the Examiner alleges that claims 8 - 11 are objected to as containing non-elected subject matter.

In the response to the restriction requirement filed May 7, 2002, Applicants elected to prosecute the subject matter of claims 8 - 11, pursuant to 35 U.S.C. § 121. It seems, however, that the Examiner has limited the scope of claim 8 to compounds where A<sub>1</sub> - A<sub>4</sub> are all carbon and A is pyrrole, based on the species that was elected, viz., 3-[(2,3-dimethylpyrrol-5-yl)-methylene]-2-indolinone. Applicants assert that this is improper since the Examiner is not following the procedure set forth in MPEP § 803.02. MPEP § 803.02 prescribes that “[f]ollowing election, the Markush-type claim will be examined fully with respect to the elected species and *further to the extent necessary to determine patentability.*” (Emphasis added). Applicants respectfully urge that the Examiner extend the search beyond the elected species as prescribed by MPEP § 803.02.

***II. Rejection under the Judicially Created Doctrine of Obviousness-type Double Patenting***

On page 3 of the Office Action, the Examiner has rejected claims 8 - 11 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 15 and 16 of U.S. Patent No. 6,313,158; and claims 1, 5, 22 and 28 of U.S. Patent No. 5,792,783. Further, the Examiner alleges that claims 8 and 9 are unpatentable over claims 1 and 3 of U.S. Patent No. 6,395,734; and claims 1 and 16 of co-pending Application No. 09/769,198.

Applicants assert that claim 8, as amended, now requires at least one of the atoms A<sub>1</sub> - A<sub>4</sub> to be a nitrogen. None of the cited patents contemplate or suggest indolinones wherein one or more atoms on the indolinone ring are nitrogen. Further, with respect to the ‘198 application, Applicants assert that one would have to pick and choose from the myriad of recited possibilities for the various rings in the genus claimed in the ‘198 application to arrive at the genus claimed in the instant application. Accordingly, the genus claimed in claim 8 is not *prima facie* obvious, in light of the teachings of U.S. Patent Nos. 6,313,158; 5,792,783; 6,395,734; and co-pending Application No. 09/769,198. Applicants therefore request reconsideration and withdrawal of the rejection.

**III. Rejection of Claims 8 under 35 U.S.C. § 112, First and Second Paragraph**

On page 4 of the Office Action the Examiner has rejected claim 1 under 35 U.S.C. § 112, first and second paragraph as being indefinite for failing to point out and distinctly claim the subject matter which applicants regard as their invention. Applicants assume that the Examiner meant to reject claim 8, under section 112 of the statute because claim 1 does not recite the language to which the Examiner objects.

In light of the amendment to claim 8, Applicants assert that this rejection has been rendered moot. Specifically, claim 8, as amended, does not recite "metabolites, esters, amides and prodrugs thereof." Reconsideration and withdrawal of the rejection is respectfully requested.

**IV. Conclusion**

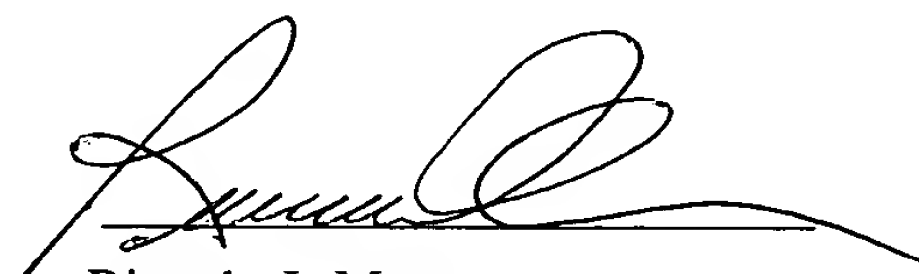
In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. Examiner Wright is invited to telephone the undersigned at the number listed below if she believes such would be helpful in advancing the application to issue.

Respectfully submitted,

*September 13, 2002*

Date

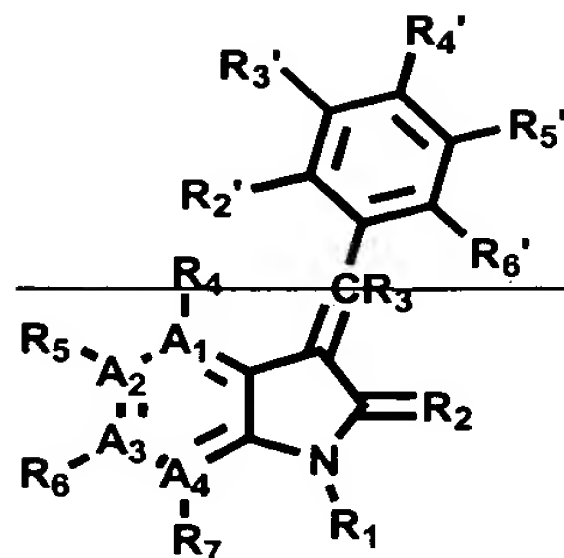
Foley & Lardner  
3000 K Street, NW  
Washington, DC 20007  
Tel: (202) 672-5300  
Fax: (202) 672-5399



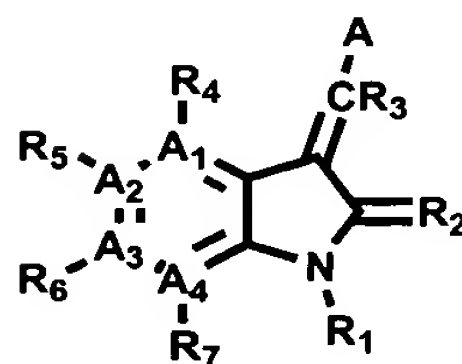
Ricardo J. Moran  
Reg. No. 48,735

**Marked-up Claim:**

8. (Amended) A compound having the formula V or VI



(V)



(VI)

or a pharmaceutically acceptable salt, ~~isomer, metabolite, ester, amide, or prodrug~~ thereof, wherein:

- (a) A<sub>1</sub>, A<sub>2</sub>, A<sub>3</sub>, and A<sub>4</sub> are independently carbon or nitrogen wherein at least one of A<sub>1</sub>, A<sub>2</sub>, A<sub>3</sub> or A<sub>4</sub> is nitrogen, it being understood that when A<sub>1</sub>, A<sub>2</sub>, A<sub>3</sub> or A<sub>4</sub> is nitrogen, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> or R<sub>7</sub> does not exist, respectively;
- (b) R<sub>1</sub> is hydrogen or alkyl;
- (c) R<sub>2</sub> is oxygen or ~~sulfersulfur~~ sulfur;
- (d) R<sub>3</sub> is hydrogen;
- (e) R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub> are optionally present and are each independently selected from (i) the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub> CO<sub>2</sub>R, and CONRR' or (ii) any two adjacent R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub> taken together form a fused ring with the aryl portion of the oxindole-based portion of the indolinone;
- ~~(f) R<sub>2</sub>', R<sub>3</sub>', R<sub>4</sub>', R<sub>5</sub>', and R<sub>6</sub>' are each independently selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub> CO<sub>2</sub>R, and CONRR';~~
- ~~(g)~~ n is 0, 1, 2, or 3;

- (hg) R is H, alkyl or aryl;
- (ih) R' is H, alkyl or aryl; and
- (ji) A is a five membered heteroaryl ring selected from the group consisting of thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, optionally substituted at one or more positions with alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R or CONRR'.